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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicant: | Cynthia C. Bamdad et al. |
| Serial No.: | 09/996,069 |
| Conf. No.: | 1136 |
| Filed: | November 27, 2001 |
| For: | Diagnostic Tumor Markers, Drug Screening for Tumorigenesis Inhibition, and Compositions and Methods for Treatment of Cancer |
| Art Unit: | 1645 |

**BOX MISSING PARTS**
Commissioner for Patents
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

This Amendment is in response to the Notice to File Missing Parts of Nonprovisional Application dated January 31, 2002. Please amend the application as follows.

**In the Specification**

**Replacement Paragraphs**

Please replace the indicated paragraphs with those shown below. A marked-up version is attached hereto with amendments indicated by bracketing (for deletions) and underlining (for insertions).

Page 22, lines 16-31.

More than one species may be a physiologically relevant ligand for this portion of the MUC1 receptor. Enzymes that modify the receptor may be relevant ligands of this portion of the receptor. For example, one ligand may bind monomerically to an unmodified MGFR portion of the MUC1 receptor, while another ligand, with a different function, such as inductive multimerization, may recognize an enzyme-modified version of the receptor. Because the experiment described above, Example 3b, was performed in

cell lysate/supernatants, it is important to note that several receptor-ligand interactions, including enzymatic modifications to the receptor, may be taking place, wherein only the ligand(s) dimerization (or multimerization) of the MGFR portion, results in a solution color change. In an experiment similar to Example 3b, (Example 8) the enzyme inhibitor, PMSF was added to the lysate prior to the introduction of the colloids bearing the synthetic peptide His-PSMGFR, see Table 1 SEQ ID NO: 2 . Referring now to Figure 20, solutions that contained PMSF did not undergo the solution color change. This result is consistent with a mechanism in which the MGFR portion of the MUC1 receptor is first enzyme mofdified before it is recognized by the ligand(s) that dimerize or multimerize the receptor.

Page 58, lines 3-7.

A histidine-tagged peptide (ESMGFR) whose sequence contained all of the amino acids in the His-PSMGFR peptide plus 9 additional amino acids from the PSIBR region, adjacent to the PSMGFR, were added to the N-terminus of the peptide.
N-terminus - VQLTLAFREGTINVHDVETQFNQYKTEAASPYNLTISDVSVS DVPFPFHHHHHH – C-terminus (SEQ ID NO:3).

Page 63, line 14 through page 64, line 12.

In an effort to identify ligands to the MUC1 receptor, synthetic, His-PSMGFR peptides,
GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGAHHHHHH (SEQ ID NO: 2), which represents the portion of the MUC1 receptor, that remains attached to the cell surface after cleavage of the interchain binding region, were loaded onto NTA-Ni beads (cat. #1000630; available from Qiagen GmbH, Germany) and incubated with cell lysates in the presence (Fig. 9) or absence (Fig. 10) of the protease inhibitor PMSF (phenyl methyl sulfonyl fluoride). Lysates from T47D cells were used because this breast tumor cell line was known to overexpress MUC1; additionally, the inventors

presented evidence herein (see Fig. 8A-D) that this cell line also overexpresses MUC1 ligand(s). T47D cells were cultured then sonicated for 1 minute to lyse the cells. Lysates were mixed with the PSMGFR peptide-presenting beads and incubated on ice with intermittent mixing for 1hr. As a negative control, an irrelevant peptide, HHHHHHRGEFTGTYITAVT (SEQ ID NO:13), was attached to NTA-Ni beads and treated identically. Both sets of beads were washed 2X with phosphate buffer pH 7.4. Bound protein species were eluted by 3 additions of 100uL of phosphate buffer that also contained 250mM imidazole. For both the peptides, a portion of the first elution was removed and reserved to run as a separate sample, while the remainder was combined with the other 2 elutions and concentrated by TCA (tri-chloro acetic acid)-precipitation (Chen, L. et al., Anal. Biochem. Vol 269; pgs 179-188; 1999). Eluates were run on a 12% SDS gel, see Figure 9. The gel was then silver stained (Schevchenko, A et al; Anal. Chem., Vol. 68; pg 850-858; 1996). Lanes were loaded as follows: (from left to right) (1) Benchmark pre-stained protein ladder (Gibco); (2) first eluate from the MUC1 peptide; (3) $1/10^{th}$ of TCA-concentrated sample; (4) blank; (5) $9/10^{th}$ TCA- concentrated sample; (6) first eluate negative control peptide; (7) $1/10^{th}$ of TCA-concentrated sample from the negative control peptide; (8) 0.5 picomoles BSA (as a standard); (9) $9/10^{th}$ TCA-concentrated sample from the negative control peptide; (10) silver stain SDS page standard (BioRad cat. #1610314). Referring now to Fig. 9, comparing lanes 2 and 6 (control), it can be seen that the MUC1 PSMGFR peptide bound distinguishably to three peptides: a first unique peptide that runs at an apparent molecular weight of 17kD; and a second peptide (more intense band) that runs at an apparent molecular weight of 23kD. Note that in lane 5, where the sample is the most concentrated, a third unique band is seen at about 35kD.

Page 67, line 15 through page 68, line 17.

Table 4

17 kD species identified herein from gel band

1) Metastasis Inhibition Factor NM23 gi: 127982

TFIAIKPDGVQR (SEQ ID NO: 14)
VM*LGETNPADSKPGTIR (SEQ ID NO: 15)
VMLGETNPADSKPGTIR (SEQ ID NO: 16)
NIIHGSDSVK (SEQ ID NO: 17)
GLVGEIIKR (SEQ ID NO: 18)
GLVGEIIK (SEQ ID NO: 19)

23 kD species identified herein from gel band
1) Metastasis Inhibition Factor NM23 gi: 127982
TFIAIKPDGVQR (SEQ ID NO: 14)
YM*HSGPVVAM*VWEGLNVVK (SEQ ID NO: 20)

35 kD identified herein from gel band
1) 14-3-3 epsilon gi: 5803225
AAFDDAIAELDTLSEESYK (SEQ ID NO: 21)
AASDIAM*TELPPTHPIR (SEQ ID NO: 22)
YLAEFATGNDR (SEQ ID NO: 23)
DSTLIMQLLR (SEQ ID NO: 24)
YDEMVESMK (SEQ ID NO: 25)
VAGM*DVELTVEER (SEQ ID NO: 26)
HLIPAANTGESK (SEQ ID NO: 27)

2) cathepsin D gi:4503143
DPDAQPGGELM*LGGTDSK (SEQ ID NO: 28)
DPDAQPGGELMLGGTDSK (SEQ ID NO: 29)
ISVNNVLPVFDNLM*QQK (SEQ ID NO: 30)
ISVNNVLPVFDNLMQQK (SEQ ID NO: 31)
QPGITFIAAK (SEQ ID NO: 32)

3) human annexin V with Proline substitution by Thrionine gi: 3212603
GLGTDEESILTLLTSR (SEQ ID NO: 33)
DLLDDLKSELTGK (SEQ ID NO: 34)
SEIDLFNIR (SEQ ID NO: 35)

Page 70, lines 1 though 28.

T47D cells were trypsinized from a T25 flask, pelleted, resuspended in phosphate buffer, and lysed by sonication to release the ligand into solution. NTA-SAM-coated colloids were bound with the His-PSMGFR peptide: GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGAHHHHHH (SEQ ID NO:2) 200µl NTA-SAM-coated colloids were incubated with 20µl 100µM peptide in phosphate buffer for 15 minutes, pelleted to remove unbound peptide, and resuspended in phosphate buffer. Negative control colloids were incubated with a random sequence histidine-tagged peptide in place of the MUC1 peptide. The cell lysate (65µl ) was mixed with 5µl drug candidate in DMSO and added to 30µl MUC1-peptide-bound colloids in the wells of an ELISA plate for a final drug concentration of approximately 100µM. Positive controls contained DMSO in place of a drug candidate; negative controls contained DMSO in place of a drug candidate, and colloids bound with a random sequence peptide in place of the MUC1 peptide. A color change from pink to blue indicates that the ligand in the cell lysate bound to the MUC1-peptide, dimerizing the peptide, and bringing the colloids into close enough proximity with one another to cause a color change. Positive controls, which do not contain a drug candidate, change color from pink to blue within two hours, as there is nothing to inhibit the interaction between the MUC1 peptide and the ligand present in the cell lysate. A lack of color change (wells remain pink) indicates that the drug candidate blocked the interaction between the MUC1 peptide and the cognate ligand, either by binding to the MGFR portion of the MUC1 receptor, inhibiting a modifying enzyme, or by binding to its activating ligand. Negative control wells, which contain colloids presenting a random sequence peptide in place of

the MUC1 peptide, remain pink, as the ligand to the MUC1 peptide will not dimerize the random sequence peptide. Figure 12 shows a sample drug-screening plate used in the assay described above. Positive control wells (A1-D1) changed color from pink to blue within two hours, while negative control wells (E1-H1) remained pink. Well E6 contains a drug that inhibited the interaction between the MUC1 peptide and the cognate ligand, causing the well to remain pink.

**In the Claims**

Please amend the claims as follows. Applicants have attached hereto pages containing amended claims, with amendments indicated by bracketing (for deletions) and underlining (for insertions).

9. (Amended) A method as in claim 4, wherein the peptide sequence is the primary sequence of the MUC1 growth factor receptor (PSMGFR).

27. (Amended) The method of claim 10, wherein the portion of the cell surface comprises at least 12 contiguous amino acids from the sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

28. (Amended) The method of claim 10, wherein the portion of the cell surface receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO: 6).

29. (Amended) The method of claim 10, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

30. (Amended) The method of claim 10, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

34. (Amended) A method as in claim 31, wherein the portion is MUC1 Growth Factor Receptor (MGFR).

35. (Amended) A method as in claim 31, wherein the portion contains a significant amount of the primary sequence of the MUC1 growth factor receptor (PFMGFR) sequence.

37. (Amended) The method of claim 31, wherein the portion of the cell surface receptor comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

38. (Amended) The method of claim 31, wherein the portion of the cell surface receptor comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

39. (Amended) The method of claim 31, wherein the specific binding portion of the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

40. (Amended) The method of claim 31, wherein the specific binding portion of the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

153. (Amended) The method of claim 151, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

163. (Amended) The method of claim 158, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

193. (Amended) The method of claim 192, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

## Remarks

This amendment is fully supported by the specification as filed. The specification has been amended to comply with 37 CFR 1.821-1.825, as requested by the Patent and Trademark Office. The claims have been amended to comply with 37 CFR 1.821-1.825 and to clarify the meaning of the abbreviations "PSMGFR" and "MGFR" which are fully defined in the specification as filed. No new matter has been added.

Applicants respectfully request the Examiner enter the amendment and the Sequence Listing attached hereto.

## Conclusion

A favorable first office action is hereby respectfully requested.

If, for any reason, the Examiner is of the opinion that a telephone conversation with Applicants' representative would expedite prosecution, the Examiner is requested to contact the undersigned at (617) 720-3500.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time.

Any fee due for an extension of time, that is not covered by an enclosed check, may be charged to Deposit Account No. 23/2825.

Respectfully submitted,

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Michael J. Pomianek, Reg. No. 46,190
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Boston, Massachusetts 02210
Tel (617) 720-3500
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**X06/30/02 (Saturday)**

**Marked-Up Specification**

Page 22, lines 16-31.

More than one species may be a physiologically relevant ligand for this portion of the MUC1 receptor. Enzymes that modify the receptor may be relevant ligands of this portion of the receptor. For example, one ligand may bind monomerically to an unmodified MGFR portion of the MUC1 receptor, while another ligand, with a different function, such as inductive multimerization, may recognize an enzyme-modified version of the receptor. Because the experiment described above, Example 3b, was performed in cell lysate/supernatants, it is important to note that several receptor-ligand interactions, including enzymatic modifications to the receptor, may be taking place, wherein only the ligand(s) dimerization (or multimerization) of the MGFR portion, results in a solution color change. In an experiment similar to Example 3b, (Example 8) the enzyme inhibitor, PMSF was added to the lysate prior to the introduction of the colloids bearing the synthetic peptide His-PSMGFR, see Table 1 SEQ ID [#]NO: 2 . Referring now to Figure 20, solutions that contained PMSF did not undergo the solution color change. This result is consistent with a mechanism in which the MGFR portion of the MUC1 receptor is first enzyme mofdified before it is recognized by the ligand(s) that dimerize or multimerize the receptor.

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A histidine-tagged peptide (ESMGFR) whose sequence contained all of the amino acids in the His-PSMGFR peptide plus 9 additional amino acids from the PSIBR region, adjacent to the PSMGFR, were added to the N-terminus of the peptide.
N-terminus - VQLTLAFREGTINVHDVETQFNQYKTEAASPYNLTISDVSVS DVPFPFHHHHHHH – C-terminus (SEQ ID NO:3).

Page 63, line 14 through page 64, line 12.

In an effort to identify ligands to the MUC1 receptor, synthetic, His-PSMGFR peptides,
GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGAHHHHHH (SEQ

ID NO: 2), which represents the portion of the MUC1 receptor, that remains attached to the cell surface after cleavage of the interchain binding region, were loaded onto NTA-Ni beads (cat. #1000630; available from Qiagen GmbH, Germany) and incubated with cell lysates in the presence (Fig. 9) or absence (Fig. 10) of the protease inhibitor PMSF (phenyl methyl sulfonyl fluoride). Lysates from T47D cells were used because this breast tumor cell line was known to overexpress MUC1; additionally, the inventors presented evidence herein (see Fig. 8A-D) that this cell line also overexpresses MUC1 ligand(s). T47D cells were cultured then sonicated for 1 minute to lyse the cells. Lysates were mixed with the PSMGFR peptide-presenting beads and incubated on ice with intermittent mixing for 1hr. As a negative control, an irrelevant peptide, HHHHHHRGEFTGTYITAVT (SEQ ID NO:13), was attached to NTA-Ni beads and treated identically. Both sets of beads were washed 2X with phosphate buffer pH 7.4. Bound protein species were eluted by 3 additions of 100uL of phosphate buffer that also contained 250mM imidazole. For both the peptides, a portion of the first elution was removed and reserved to run as a separate sample, while the remainder was combined with the other 2 elutions and concentrated by TCA (tri-chloro acetic acid)-precipitation (Chen, L. et al., Anal. Biochem. Vol 269; pgs 179-188; 1999). Eluates were run on a 12% SDS gel, see Figure 9. The gel was then silver stained (Schevchenko, A et al; Anal. Chem., Vol. 68; pg 850-858; 1996). Lanes were loaded as follows: (from left to right) (1) Benchmark pre-stained protein ladder (Gibco); (2) first eluate from the MUC1 peptide; (3) $1/10^{th}$ of TCA-concentrated sample; (4) blank; (5) $9/10^{th}$ TCA- concentrated sample; (6) first eluate negative control peptide; (7) $1/10^{th}$ of TCA-concentrated sample from the negative control peptide; (8) 0.5 picomoles BSA (as a standard); (9) $9/10^{th}$ TCA-concentrated sample from the negative control peptide; (10) silver stain SDS page standard (BioRad cat. #1610314). Referring now to Fig. 9, comparing lanes 2 and 6 (control), it can be seen that the MUC1 PSMGFR peptide bound distinguishably to three peptides: a first unique peptide that runs at an apparent molecular weight of 17kD; and a second peptide (more intense band) that runs at an apparent molecular weight of 23kD.

Note that in lane 5, where the sample is the most concentrated, a third unique band is seen at about 35kD.

Page 67, line 15 through page 68, line 17.
Table 4

17 kD species identified herein from gel band

1) Metastasis Inhibition Factor NM23 gi: 127982

TFIAIKPDGVQR (SEQ ID NO: 14)

VM*LGETNPADSKPGTIR (SEQ ID NO: 15)

VMLGETNPADSKPGTIR (SEQ ID NO: 16)

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GLVGEIIK (SEQ ID NO: 19)

23 kD species identified herein from gel band

1) Metastasis Inhibition Factor NM23 gi: 127982

TFIAIKPDGVQR (SEQ ID NO: 14)

YM*HSGPVVAM*VWEGLNVVK (SEQ ID NO: 20)

35 kD identified herein from gel band

1) 14-3-3 epsilon gi: 5803225

AAFDDAIAELDTLSEESYK (SEQ ID NO: 21)

AASDIAM*TELPPTHPIR (SEQ ID NO: 22)

YLAEFATGNDR (SEQ ID NO: 23)

DSTLIMQLLR (SEQ ID NO: 24)

YDEMVESMK (SEQ ID NO: 25)

VAGM*DVELTVEER (SEQ ID NO: 26)

HLIPAANTGESK (SEQ ID NO: 27)

2) cathepsin D gi:4503143

DPDAQPGGELM*LGGTDSK (SEQ ID NO: 28)
DPDAQPGGELMLGGTDSK (SEQ ID NO: 29)
ISVNNVLPVFDNLM*QQK (SEQ ID NO: 30)
ISVNNVLPVFDNLMQQK (SEQ ID NO: 31)
QPGITFIAAK (SEQ ID NO: 32)

3) human annexin V with Proline substitution by Thrionine gi: 3212603
GLGTDEESILTLLTSR (SEQ ID NO: 33)
DLLDDLKSELTGK (SEQ ID NO: 34)
SEIDLFNIR (SEQ ID NO: 35)

Page 70, lines 1 though 28.

T47D cells were trypsinized from a T25 flask, pelleted, resuspended in phosphate buffer, and lysed by sonication to release the ligand into solution. NTA-SAM-coated colloids were bound with the His-PSMGFR peptide: GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGAHHHHHH (SEQ ID NO:2) 200µl NTA-SAM-coated colloids were incubated with 20µl 100µM peptide in phosphate buffer for 15 minutes, pelleted to remove unbound peptide, and resuspended in phosphate buffer. Negative control colloids were incubated with a random sequence histidine-tagged peptide in place of the MUC1 peptide. The cell lysate (65µl ) was mixed with 5µl drug candidate in DMSO and added to 30µl MUC1-peptide-bound colloids in the wells of an ELISA plate for a final drug concentration of approximately 100µM. Positive controls contained DMSO in place of a drug candidate; negative controls contained DMSO in place of a drug candidate, and colloids bound with a random sequence peptide in place of the MUC1 peptide. A color change from pink to blue indicates that the ligand in the cell lysate bound to the MUC1-peptide, dimerizing the peptide, and bringing the colloids into close enough proximity with one another to cause a color change. Positive controls, which do not contain a drug candidate, change color from pink to blue within two hours, as there is nothing to inhibit the interaction between

the MUC1 peptide and the ligand present in the cell lysate. A lack of color change (wells remain pink) indicates that the drug candidate blocked the interaction between the MUC1 peptide and the cognate ligand, either by binding to the MGFR portion of the MUC1 receptor, inhibiting a modifying enzyme, or by binding to its activating ligand. Negative control wells, which contain colloids presenting a random sequence peptide in place of the MUC1 peptide, remain pink, as the ligand to the MUC1 peptide will not dimerize the random sequence peptide. Figure 12 shows a sample drug-screening plate used in the assay described above. Positive control wells (A1-D1) changed color from pink to blue within two hours, while negative control wells (E1-H1) remained pink. Well E6 contains a drug that inhibited the interaction between the MUC1 peptide and the cognate ligand, causing the well to remain pink.

**Marked-Up Claims**

10. (Amended) A method as in claim 4, wherein the peptide sequence is the primary sequence of the MUC1 growth factor receptor (PSMGFR).

27. (Amended) The method of claim 10, wherein the portion of the cell surface comprises at least 12 contiguous amino acids from the sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

28. (Amended) The method of claim 10, wherein the portion of the cell surface receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO: 6).

29. (Amended) The method of claim 10, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

30. (Amended) The method of claim 10, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

34. (Amended) A method as in claim 31, wherein the portion is MUC1 Growth Factor Receptor (MGFR).

35. (Amended) A method as in claim 31, wherein the portion contains a significant amount of the primary sequence of the MUC1 growth factor receptor (PFMGFR) sequence.

37. (Amended) The method of claim 31, wherein the portion of the cell surface receptor comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

38. (Amended) The method of claim 31, wherein the portion of the cell surface receptor comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

39. (Amended) The method of claim 31, wherein the specific binding portion of the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

40. (Amended) The method of claim 31, wherein the specific binding portion of the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

154. (Amended) The method of claim 151, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

163. (Amended) The method of claim 158, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

193. (Amended) The method of claim 192, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

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**Date of Deposit: July 1, 2002**

**Attorney Docket No: M01015/70071 TJO/MJP**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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|---|---|
| Applicant(s): | Cynthia C. Bamdad et al. |
| Serial No: | 09/996,069 |
| Conf. No.: | 1136 |
| Filing Date: | November 27, 2001 |
| For: | DIAGNOSTIC TUMOR MARKERS, DRUG SCREENING FOR TUMORIGENESIS INHIBITION, AND COMPOSITIONS AND METHODS FOR TREATMENT OF CANCER |
| Examiner: | Not Yet Assigned |
| Art Unit: | 1645 |

**CERTIFICATE OF EXPRESS MAILING UNDER 37 C.F.R. §1.8(a)**

The undersigned hereby certifies that this document is being placed in the United States mail via express mail, addressed to U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202, on the 1st day of July, 2002.

Tina Hanifin

Attn: Official Draftsperson
Commissioner for Patents
Washington, DC 20231

**LETTER TO OFFICIAL DRAFTSPERSON**

Sir:

Subject to the approval of the Examiner in this case, enclosed for filing are twenty three (23) sheets of FORMAL DRAWINGS, Figures 1 through 20, for the above-referenced patent application.

The Commissioner is hereby authorized to charge any fees which may be required to Deposit Account No. 23-2825. A duplicate of this sheet is enclosed.

Respectfully submitted,
***Cynthia C. Bamdad et al., Applicant(s)***

By: _____

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Timothy J. Oyer, Reg. No. 36,628
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**xNDD**

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